

09/836, 712
1812

FIG.1

CCGGGTGACCCACGCGTCCGAAGGCCCCCTCTCACTCCGCTCCACTCCTCGGGCTGG
5 CTCTCCTGAGGATGCACCAGCGTCACCCCCGGGCAAGATGCCCTCCCCTCTGTGTGGC
CGGAATCCTTGCCTGTGGCTTTCTCCTGGGCTGCTGGGGACCCTCCCATTTCCAGCAGA
GTTGTCTTCAGGCTTTGGAGCCACAGGCCGTGTCTTCTTACTTGAGCCCTGGTGCTCCC
TTAAAAGGCCGCCCTCCTTCCCCTGGCTTCCAGAGGCAGAGGCAGAGGCAGAGGCAGGCGGG
CTGCAGGCGGCATCCTACACCTGGAGCTGCTGGTGGCCGTGGGCCCCGATGTCTTCCA
10 GGCTCACCAGGAGGACACAGAGCGCTATGTGCTACCAACCTCAACATCGGGGCAGAA
CTGCTTCGGGACCCGTCCCTGGGGGCTCAGTTTCGGGTGCACCTGGTGAAGATGGTCA
TTCTGACAGAGCCTGAGGGTGCTCCAAATATCACAGCCAACCTCACCTCGTCCCTGCTG
AGCGTCTGTGGGTGGAGCCAGACCATCAACCCTGAGGACGACACGGATCCTGGCCATG
CTGACCTGGTCTCTATATCACTAGGTTTGACCTGGAGTTGCCTGATGGTAACCGGCAG
15 GTGCGGGGCGTCACCCAGCTGGGCGGTGCCTGCTCCCCAACCTGGAGCTGCCTCATT
CCGAGGACACTGGCTTCGACCTGGGAGTCACCATTGCCCATGAGATTGGGCACAGCTT
CGGCCTGGAGCACGACGGCGCGCCCCGGCAGCGGCTGCGGCCCCAGCGGACACGTGA
TGGCTTCGGACGGCGCCGCGCCCCGCGCGGCTCGCCTGGTCCCCCTGCAGCCGCC
GGCAGCTGCTGAGCCTGCTCAGCGCAGGACGGGCGCGCTGCGTGTGGGACCCGCGCGC
20 GGCTCAACCCGGGTCCGCGGGGACCCGCGCGGATGCGCAGCCTGGCCTCTACTACA
GCGCCAACGAGCAGTGCCGCGTGGCCTTCGGCCCCAAGGCTGTGCGCTGCACCTTCGC
CAGGGAGCACCTGGATATGTGCCAGGCCCTCTCCTGCCACACAGACCCGCTGGACCAA
AGCAGCTGCAGCCGCCTCCTCGTTCTCCTTGATGGGACAGAATGTGGCGTGGAGA
AGTGGTGCTCCAAGGGTCGCTGCCGCTCCCTGGTGGAGCTGACCCCCATAGCAGCAGT
25 GCATGGGCGCTGGTCTAGCTGGGGTCCCCGAAGTCCTTGCTCCCGCTCCTGCGGAGGA
GGTGTGGTCACCAGGAGGCGGCAGTGCAACAACCCAGACCTGCCTTTGGGGGGCGT
GCATGTGTTGGTGCTGACCTCCAGGCCGAGATGTGCAACACTCAGGCCTGCGAGAAGA
CCCAGCTGGAGTTCATGTGCAACAGTGCGCCAGGACCGACGGCCAGCCGCTGCGCTC
CTCCCCCTGGCGGCGCCTCCTTCTACCACTGGGGTGCTGCTGTACCACACAGCCAAGGG
30 GATGCTCTGTGCAGACACATGTGCCGGGCCATTGGCGAGAGCTTCATCATGAAGCGTG
GAGACAGCTTCCTCGATGGGACCCGGTGTATGCCAAGTGGCCCCCGGGAGGACGGGA
CCCTGAGCCTGTGTGTGTCGGGCAGCTGCAGGACATTTGGCTGTGATGGTAGGATGGA
CTCCCAGCAGGTATGGGACAGGTGCCAGGTGTGTGGTGGGGACAACAGCACGTGCAGC
CCACGGAAGGGCTCTTTCACAGCTGGCAGAGCGAGAGAATATGTCACGTTTCTGACAGT
35 TACCCCCAACCTGACCAGTGTCTACATTGCCAACACAGGCCTCTCTTCACACACTTGG
CGGTGAGGATCGGAGGGCGCTATGTCGTGGCTGGGAAGATGAGCATCTCCCCTAACAC
CACCTACCCCTCCCTCCTGGAGGATGGTTCGTGTCGAGTACAGAGTGGCCCTCACCGAG

Substituted

EXPRESS MAIL # EM 51111419745

09/836, 712
2 of 12

TCF02Z9860

GACCGGCTGCCCCGCCTGGAGGAGATCCGCATCTGGGGACCCCTCCAGGAAGATGCT
GACATCCAGGTTTACAGGCGGTATGGCGAGGAGTATGGCAACCTCACCCGCCAGACA
TCACCTTCACCTACTTCCAGCCTAAGCCACGGCAGGCCTGGGTGTGGGCCGCTGTGCG
TGGGCCCTGCTCGGTGAGCTGTGGGGCAGGGCTGCGCTGGGTAAACTACAGCTGCCTG
5 GACCAGGCCAGGAAGGAGTTGGTGGAGACTGTCCAGTGCCAAGGGAGCCAGCAGCCA
CCAGCGTGGCCAGAGGCCTGCGTGCTCGAACCCTGCCCTCCCTACTGGGCGGTGGGA
GACTTCGGCCCATGCAGCGCCTCCTGTGGGGGTGGCCTGCGGGAGCGGCCAGTGCGC
TGCGTGGAGGCCAGGGCAGCCTCCTGAAGACATTGCCCCAGCCCGGTGCAGAGCA
GGGGCCCAGCAGCCAGCTGTGGCGCTGGAAACCTGCAACCCCCAGCCCTGCCCTGCC
10 AGGTGGGAGGTGTCAGAGCCCAGCTCATGCACATCAGCTGGTGGAGCAGGCCTGGCCT
TGGAGAACGAGACCTGTGTGCCAGGGGCAGATGGCCTGGAGGCTCCAGTGACTGAGG
GGCCTGGCTCCGTAGATGAGAAGCTGCCTGCCCCTGAGCCCTGTGTCTGGGATGTCATG
TCCTCCAGGCTGGGGCCATCTGGATGCCACCTCTGCAGGGGAGAAGGCTCCCTCCCCA
TGGGGCAGCATCAGGACGGGGGCTCAAGCTGCACACGTGTGGACCCCTGCGGCAGGG
15 TCGTGCTCCGTCTCCTGCGGGCGAGGTCTGATGGAGCTGCGTTTCCTGTGCATGGACT
CTGCCCTCAGGGTGCCTGTCCAGGAAGAGCTGTGTGGCCTGGCAAGCAAGCCTGGGAG
CCGGCGGGAGGTCTGCCAGGCTGTCCCGTGCCCTGCTCGGTGGCAGTACAAGCTGGC
GGCCTGCAGCGTGAGCTGTGGGAGAGGGGTGCTGCGGAGGATCCTGTATTGTGCCCG
GGCCCATGGGGAGGACGATGGTGAGGAGATCCTGTTGGACACCCAGTGCCAGGGGCT
20 GCCTCGCCCGGAACCCAGGAGGCCTGCAGCCTGGAGCCCTGCCACCTAGGTGGAA
AGTCATGTCCCTTGGCCCATGTTGCGCCAGCTGTGGCCTTGGCACTGCTAGACGCTCG
GTGGCCTGTGTGCAGCTCGACCAAGGCCAGGACGTGGAGGTGGACGAGGCGGCCTGT
GCGGCGCTGGTGCGGCCCGAGGCCAGTGTCCCCTGTCTCATTGCCGACTGCACCTACC
GCTGGCATGTTGGCACCTGGATGGAGTGCTCTGTTTCCTGTGGGGATGGCATCCAGCG
25 CCGGCGTGACACCTGCCTCGGACCCCAGGCCAGGCGCCTGTGCCAGCTGATTTCTGC
CAGCACTTGCCCAAGCCGGTGA CTGTGCGTGGCTGCTGGGCTGGGCCCTGTGTGGGAC
AGGGTACGCCCAGCCTGGTGCCCCACGAAGAAGCCGCTGCTCCAGGACGGACCACAG
CCACCCCTGCTGGTGCCTGTGGCAGGCAGCACCTTGAGCCAACAGGAACCATTGACAT
GCGAGGCCAGGGCAGGCAGACTGTGCAGTGGCCATTGGGCGGCCCTCGGGGAGGT
30 GGTGACCCTCCGCGTCCTTGAGAGTTCTCTCAACTGCAGTGCGGGGGACATGTTGCTG
CTTTGGGGCCGGCTCACCTGGAGGAAGATGTGCAGGAAGCTGTTGGACATGACTTTCA
GCTCCAAGACCAACACGCTGGTGGTGAGGCAGCGCTGCGGGCGGCCAGGAGGTGGGG
TGCTGCTGCGGTATGGGAGCCAGCTTGCTCCTGAAACCTTCTACAGAGAATGTGACATG
CAGCTCTTTGGGCCCTGGGGTGAAATCGTGAGCCCCTCGCTGAGTCCAGCCACGAGTA
35 ATGCAGGGGGCTGCCGGCTCTTCATTAATGTGGCTCCGCACGCACGGATTGCCATCCAT
GCCCTGGCCACCAACATGGGCGCTGGGACCGAGGGAGCCAATGCCAGCTACATCTTGA
TCCGGGACACCCACAGCTTGAGGACCACAGCGTTCCATGGGCAGCAGGTGCTCTACTG

09/836, 712
3 of 12

GGAGTCAGAGAGCAGCCAGGCTGAGATGGAGTTCAGCGAGGGCTTCCTGAAGGCTCAG
GCCAGCCTGCGGGGCCAGTACTGGACCCTCCAATCATGGGTACCGGAGATGCAGGACC
CTCAGTCCTGGAAGGGAAAGGAAGGAACC

09836712-044704

09/836, 712
4 of 12

FIG. 2

5

PGRPTRPKAPSHSAPLLGLALLRMHQRHPRARCPPLCVAGILACGFLGCGWGPSHFQQSCL
QALEPQAVSSYLSPGAPLKGRPPSPGFQRQRQRRAAGGILHLELLVAVGPDVFQAHQED
TERYVLTNLNIGAELLRDPSTLGAQFRVHLVKMVILTEPEGAPNITANLTSSLLSVCGWSQTINP
EDDTPDGHADLVLYITRFDLELPDGNRQVRGVTQLGGACSTWVSLITEDTGFDLGVTIAHEI

10

GHSFGLHDGAPGSGCGPSGHVMASDGAAPRAGLAWSPCSRRLSLLSAGRARCWVDP
PRPQPGSAGHPPDAQPGLYYSANEQCRVAFGPKAVACTFAREHLDMCQALSCHTDPLDQS
SCSRLLVPLLDGTECGVEKWCSKGRCSRSLVELTPIAAVHGRWSSWGPRSPCSRSCGGGVV
TRRRQCNNPRPAFGGRACVGADLQAEMCNTQACEKTQLEFMSQQCARTDGQPLRSSPGG
ASFYHWGAAPVPHSQGDALCRHMCRAIGESFIMKRGDSFLDGTTRCMPSPREDGTLSLCVS

15

GSCRTFGCDGRMDSQQVWDRQCQVCGGDNSTCSPRKGSFTAGRAREYVFTLTVTPNLTSTV
YIANHRPLFTHLAVRIGGRYVVAGKMSISPNTTYPSSLLEDGRVEYRVALTEDRLPRLEEIRIWG
PLQEDADIQVYRRYGEYGNLTRPDITFTYFQPKPRQAWVWAAVRGPCSVSAGLRWVN
YSCLDQARKELVETVQCQGSQQPPAWPEACVLEPCPPYWAVGDFGPCSASCGGGLRERP
VRCVEAQGSLLKTLPPARCRAGAQQPAVALETCPNPQPCPARWEVSEPSSCTSAGGAGLAL

20

ENETCVPGADGLEAPVTEGPGSVDEKLPAPEPCVGMSCPPGWGHLDATSAGEKAPSPWG
SIRTGAQAAHVWTPAAGSCSVSCGRGLMELRFLCMDALRVPVQEELCGLASKPGSRREV
CQAVPCPARWQYKLAACSVSCGRGVVRRILYCARAHGEDDGEEILLDTQCQGLRPEPQE
ACSLEPCPPRWKVMSLGPCSASCGLGTARRSVACVQLDQGGQDVEVDEAACAALVRPEASV
PCLADCTYRWHVGTWMECSVSCGDGIQRRRTCLGPQAQAPVPADFCQHLPKPVTVRGC

25

WAGPCVGGQTSLVPHEEAAAPGRTTATPAGACGRQHLEPTGTIDMRGPGQADCAVAIGR
PLGEVVTLRVLESSLNCSAGDMLLLWGRLTWRKMCRKLLDMTFSSKTNTLVVRQRCGRPG
GGVLLRYGSQLAPETFYRECDMQLFGPWGEIVSPSLSPATSNAGGCRLFINVAPHARIAHAL
ATNMGAGTEGANASYILIRDTHSLRTTAFHGQQVLYWESESSQAEMEFSEGFLKAQASLRG
QYWTLQSWVPEMQDPQSWKGKEGT

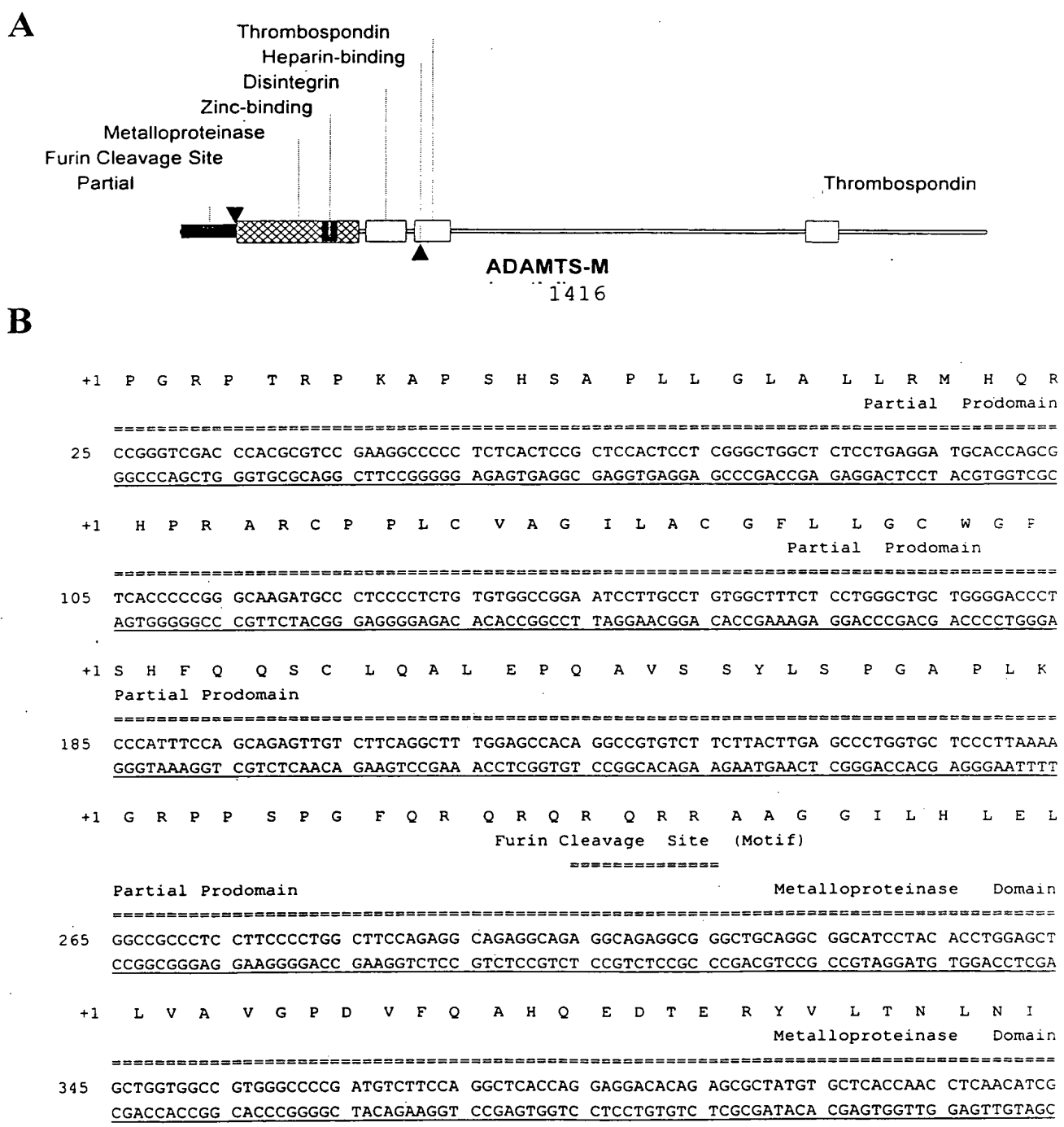
30

09/836, 712

09/836,712
5/12

Figure 3

Domain structure of ADAMTS-M and translated nucleic acid sequence. A) Diagram of ADAMTS-M showing the following domains and signature motifs (with amino acid numbers in parentheses): partial prodomain (1-97), furin cleavage site (94-97), metalloproteinase domain (98-311), zinc-binding motif (247-272), disintegrin domain (324-394), thrombospondin submotifs (410-473 and 1099-1156), and a heparin-binding motif (419-424). B) ADAMTS-M nucleotide sequence with translated amino acid sequence above.



09/23/12
6 of 12

+1 G A E L L R D P S L G A Q F R V H L V K M V I L T E P
Metalloproteinase Domain
=====

425 GGGCAGAACT GCTTCGGGAC CCGTCCTGG GGGCTCAGTT TCGGGTGAC CTGGTGAAGA TGGTCATTCT GACAGAGCCT
CCCGTCTTGA CGAAGCCCTG GGCAGGGACC CCCGAGTCAA AGCCACGCTG GACCACTTCT ACCAGTAAGA CTGTCTCGGA

+1 E G A P N I T A N L T S S L L S V C G W S Q T I N P E
Metalloproteinase Domain
=====

505 GAGGGTGCTC CAAATATCAC AGCCAACCTC ACCTCGTCCC TGCTGAGCGT CTGTGGGTGG AGCCAGACCA TCAACCTGA
CTCCCACGAG GTTTATAGTG TCGGTTGGAG TGGAGCAGGG ACGACTCGCA GACACCCACC TCGGTCTGGT AGTTGGGACT

+1 D D T D P G H A D L V L Y I T R F D L E L P D G N R
Metalloproteinase Domain
=====

585 GGACGACACG GATCCTGGCC ATGCTGACCT GGTCTCTAT ATCACTAGGT TTGACCTGGA GTTGCTGAT GGTAACCGGC
CCTGCTGTGC CTAGGACCGG TACGACTGGA CCAGGAGATA TAGTGATCCA AACTGGACCT CAACGGACTA CCATTGGCCG

+1 Q V R G V T Q L G G A C S P T W S C L I T E D T G F D
Metalloproteinase Domain
=====

665 AGGTGCGGGG CGTCACCCAG CTGGGCGGTG CCTGCTCCC AACCTGGAGC TGCTCATT A CCGAGGACAC TGGCTTCGAC
TCCACGCCCC GCAGTGGGTC GACCCGCCAC GGACGAGGGG TTGGACCTCG ACGGAGTAAT GGCTCCTGTG ACCGAAGCTG

+1 L G V T I A H E I G H S F G L E H D G A P G S G C G P
Zinc-binding Motif
=====

Metalloproteinase Domain
=====

745 CTGGGAGTCA CCATTGCCCA TGAGATTGGG CACAGCTTCG GCCTGGAGCA CGACGGCGCG CCCGGCAGCG GCTGCGGCC
GACCCTCAGT GGTAACGGGT ACTCTAAGCC GTGTCGAAGC CGGACCTCGT GTGCGCGCG GGGCCGTCG CGACGCGCG

+1 S G H V M A S D G A A P R A G L A W S P C S R R Q L
Zinc-binding Motif
=====

Metalloproteinase Domain
=====

825 CAGCGGACAC GTGATGGCTT CGGACGGCGC CGCGCCCCGC GCCGGCCTCG CCTGGTCCC CTGCAGCCGC CGGCAGCTGC
GTCGCCTGTG CACTACCGAA GCCTGCCGCG GCGCGGGGCG CGGCCGGAGC GGACCAGGGG GACGTCGGCG GCCGTCGACG

+1 L S L L S A G R A R C V W D P P R P Q P G S A G H P P
Metalloproteinase Domain
=====

905 TGAGCCTGCT CAGCGCAGGA CGGGCGCGCT GCGTGTGGGA CCCGCCGCGG CCTCAACCCG GGTCCGCGGG GCACCCGCGG
ACTCGGACGA GTCGCGTCTT GCCCGCGCGA CGCACACCCT GGGCGGCGCC GGAGTTGGGC CCAGGCGCCC CGTGGGCGCG

+1 D A Q P G L Y Y S A N E Q C R V A F G P K A V A C T F
Disintegrin Domain
=====

985 GATGCGCAGC CTGGCCTCTA CTACAGCGCC AACGAGCAGT GCCGCGTGGC CTTCGGCCCC AAGGTGTGCG CTGCACCTT
CTACGCGTCG GACCGGAGAT GATGTCGCGG TTGCTCGTCA CGGCGCACCG GAAGCCGGGG TTCCGACAGC GGACGTGGAA

09/23/12

09/836,712
7 of 12

+1 A R E H L D M C Q A L S C H T D P L D Q S S C S R L
Disintegrin Domain
=====

1065 CGCCAGGGAG CACCTGGATA TGTGCCAGGC CCTCTCCTGC CACACAGACC CGCTGGACCA AAGCAGCTGC AGCCGCCTCC
GCGGTCCCTC GTGGACCTAT ACACGGTCCG GGAGAGGACG GTGTGTCTGG GCGACCTGGT TTCGTCGACG TCGGCGGAGG

+1 L V P L L D G T E C G V E K W C S K G R C R S L V E L
Disintegrin Domain
=====

1145 TCGTTCCTCT CCTGGATGGG ACAGAATGTG GCGTGGAGAA GTGGTGCTCC AAGGGTCGCT GCCGCTCCCT GGTGGAGCTG
AGCAAGGAGA GGACCTACCC TGTCTTACAC CGCACCTCTT CACCACGAGG TCCCAGCGA CGGCGAGGGA CCACCTCGAC

+1 T P I A A V H G R W S S W G P R S P C S R S C G G G V
Heparin-binding Motif
=====

Thrombospondin Submotif
=====

1225 ACCCCCATAG CAGCAGTGCA TGGGCGCTGG TCTAGCTGGG GTCCCCAAG TCCTTGCTCC CGCTCCTGCG GAGGAGGTGT
TGGGGGTATC GTCGTCACGT ACCCGCGACC AGATCGACCC CAGGGGCTTC AGGAACGAGG GCGAGGACGC CTCTCCACA

+1 V T R R R Q C N N P R P A F G G R A C V G A D L Q A
Thrombospondin Submotif
=====

1305 GGTCACCAGG AGGCGGCAGT GCAACAACCC CAGACCTGCC TTTGGGGGGC GTGCATGTGT TGGTGCTGAC CTCCAGGCCG
CCAGTGCTCC TCCGCCGTCA CGTTGTTGGG GTCTGGACGG AAACCCCCG CACGTACACA ACCACGACTG GAGGTCCGGC

+1 E M C N T Q A C E K T Q L E F M S Q Q C A R T D G Q P
Thrombospondin Submotif
=====

1385 AGATGTGCAA CACTCAGGCC TGCAGAGAAGA CCCAGCTGGA GTTCATGTCG CAACAGTGCG CCAGGACCGA CGGCCAGCCG
TCTACACGTT GTGAGTCCGG ACGCTCTTCT GGGTCGACCT CAAGTACAGC GTTGTCACGC GGTCTGGCT GCCGGTCCGG

+1 L R S S P G G A S F Y H W G A A V P H S Q G D A L C R
1465 CTGCGCTCCT CCCCTGGCGG CGCCTCCTTC TACCACTGGG GTGCTGCTGT ACCACACAGC CAAGGGGATG CTCTGTGACG
GACGCGAGGA GGGGACCGCC GCGGAGGAAG ATGGTGACCC CACGACGACA TGGTGCTGCG GTTCCCCTAC GAGACACGTC

+1 H M C R A I G E S F I M K R G D S F L D G T R C M P
1545 ACACATGTGC CGGGCCATTG GCGAGAGCTT CATCATGAAG CGTGGAGACA GCTTCCTCGA TGGGACCCGG TGTATGCCAA
TGTGTACACG GCCCGGTAAC CGCTCTCGAA GTAGTACTTC GCACCTCTGT CGAAGGAGCT ACCCTGGGCC ACATACGGTT

+1 S G P R E D G T L S L C V S G S C R T F G C D G R M D
1625 GTGGCCCCCG GGAGGACGGG ACCCTGAGCC TGTGTGTGTC GGGCAGCTGC AGGACATTTG GCTGTGATGG TAGGATGGAC
CACCGGGGGC CCTCCTGCCC TGGGACTCGG ACACACACAG CCCGTCGACG TCCTGTAAAC CGACACTACC ATCCTACCTG

+1 S Q Q V W D R C Q V C G G D N S T C S P R K G S F T A
1705 TCCCAGCAGG TATGGGACAG GTGCCAGGTG TGTGGTGGGG ACAACAGCAC GTGCAGCCCA CGGAAGGGCT CTTTCACAGC
AGGGTCGTCC ATACCCTGTC CACGGTCCAC ACACCACCCC TGTTGTCGTG CACGTCGGGT GCCTTCCCGA GAAAGTGTCTG

+1 G R A R E Y V T F L T V T P N L T S V Y I A N H R P
1785 TGGCAGAGCG AGAGAATATG TCACGTTTCT GACAGTTACC CCCAACCTGA CCAGTGTCTA CATTGCCAAC CACAGGCCTC
ACCGTCTCGC TCTCTTATAC AGTGCAAAGA CTGTCAATGG GGGTGGACT GGTACAGAT GTAACGGTTG GTGTCCGGAG

09836712:04704

09/836,712
8 of 12

+1 L F T H L A V R I G G R Y V V A G K M S I S P N T T Y
1865 TCTTCACACA CTTGGCGGTG AGGATCGGAG GGCCTATGT CGTGGCTGGG AAGATGAGCA TCTCCCCTAA CACCACCTAC
AGAAGTGTGT GAACCGCCAC TCCTAGCCTC CCGCGATACA GCACCGACCC TTCTACTCGT AGAGGGGATT GTGTGGGATG

+1 P S L L E D G R V E Y R V A L T E D R L P R L E E I R
1945 CCCTCCCTCC TGGAGGATGG TCGTGTGAG TACAGAGTGG CCCTCACCAG GGACCGGCTG CCCCGCTGG AGGAGATCCG
GGGAGGGAGG ACCTCCTACC AGCACAGCTC ATGTCTCACC GGGAGTGGCT CCTGGCCGAC GGGGCGGACC TCCTTAGG

+1 I W G P L Q E D A D I Q V Y R R Y G E E Y G N L T R
2025 CATCTGGGGA CCCCTCCAGG AAGATGCTGA CATCCAGGTT TACAGGCGGT ATGGCGAGGA GTATGGCAAC CTCACCCGCC
GTAGACCCCT GGGGAGGTCC TTCTACGACT GTAGGTCCAA ATGTCCGCCA TACCGCTCCT CATACCGTTG GAGTGGGCGG

+1 P D I T F T Y F Q P K P R Q A W V W A A V R G P C S V
2105 CAGACATCAC CTTACCTAC TTCCAGCCTA AGCCACGGCA GGCCTGGGTG TGGGCGCTG TGCCTGGGCC CTGCTCGGTG
GTCTGTAGTG GAAGTGGATG AAGGTCGGAT TCGGTGCCGT CCGGACCCAC ACCGCGCGAC ACGACCCCGG GACGAGCCAC

+1 S C G A G L R W V N Y S C L D Q A R K E L V E T V Q C
2185 AGCTGTGGGG CAGGGCTGCG CTGGGTAAAC TACAGCTGCC TGGACCAGGC CAGGAAGGAG TTGGTGGAGA CTGTCCAGTG
TCGACACCCC GTCCCGACGC GACCCATTG ATGTGACGG ACCTGGTCCG GTCCTTCCTC AACCACTCT GACAGGTAC

+1 Q G S Q Q P P A W P E A C V L E P C P P Y W A V G D
2265 CCAAGGGAGC CAGCAGCCAC CAGCGTGGCC AGAGGCTGC GTGCTCGAAC CCTGCCCTCC CTACTGGGCG GTGGGAGACT
GGTCCCTCG GTCGTCGGTG GTCGCACCGG TCTCCGACG CACGAGCTTG GGACGGGAGG GATGACCCGC CACCTCTGA

+1 F G P C S A S C G G G L R E R P V R C V E A Q G S L L
2345 TCGGCCATG CAGCGCCTCC TGTGGGGTG GCCTGCGGGA GCGGCCAGTG CGCTGCGTGG AGGCCAGGG CAGCCTCCTG
AGCCGGGTAC GTCGCGGAGG ACACCCCCAC CGGACGCCCT CGCCGGTCAC GCGACGCACC TCCGGGTCCC GTCGGAGGAC

+1 K T L P P A R C R A G A Q Q P A V A L E T C N P Q P C
2425 AAGACATTGC CCCAGCCCC GTGCAGAGCA GGGGCCAGC AGCCAGTGT GGCCTGGAA ACCTGCAACC CCCAGCCCTG
TTCTGTAACG GGGGTCGGGC CACGTCTCGT CCCCCTGCG TCGGTGACA CCGCGACCTT TGGACGTTG GGGTCGGGAC

+1 P A R W E V S E P S S C T S A G G A G L A L E N E T
2505 CCCTGCCAGG TGGGAGGTGT CAGAGCCCAG CTCATGCACA TCAGCTGGTG GAGCAGGCTT GGCTTGGAG AACGAGACCT
GGGACGGTCC ACCCTCCACA GTCTCGGGT GAGTACGTT AGTCGACCAC CTCGTCCGA CCGGAACCTC TTGCTCTGGA

+1 C V P G A D G L E A P V T E G P G S V D E K L P A P E
2585 GTGTGCCAGG GGCAGATGGC CTGGAGGCTC CAGTACTGA GGGGCTGGC TCCGTAGATG AGAAGCTGCC TGCCCTGAG
CACACGGTCC CCGTCTACCG GACCTCCGAG GTCACTGACT CCCCAGGAC AGGCATCTAC TCTTCGACG ACGGGGACTC

+1 P C V G M S C P P G W G H L D A T S A G E K A P S P W
2665 CCCTGTGTCG GGATGTCATG TCCTCCAGGC TGGGGCCATC TGGATGCCAC CTCTGCAGGG GAGAAGGCTC CCTCCCCATG
GGGACACAGC CCTACAGTAC AGGAGGTCCG ACCCCGGTAG ACCTACGGTG GAGACGTCCC CTCTCCGAG GGAGGGGTAC

+1 G S I R T G A Q A A H V W T P A A G S C S V S C G R
2745 GGGCAGCATC AGGACGGGG CTCAAGCTGC ACACGTGTGG ACCCTGCGG CAGGGTCGTG CTCCGTCTCC TGCGGGCGAG
CCCGTCGTAG TCCTGCCCC GAGTTCGACG TGTGCACACC TGGGGACGCC GTCCAGCAC GAGGCAGAGG ACGCCCGCTC

+1 G L M E L R F L C M D S A L R V P V Q E E L C G L A S
2825 GTCTGATGGA GCTGCGTTTC CTGTGCATGG ACTCTGCCCT CAGGGTGCTT GTCCAGGAAG AGCTGTGTGG CCTGGCAAGC
CAGACTACCT CGACGCAAAG GACACGTACC TGAGACGGGA GTCCACGGA CAGGTCTTC TCGACACACC GGACCGTTCC

09/836,712
8 of 12

[illegible]

+1 K P G S R E T R E V C Q A V P C P A R W Q Y K L A A C S V
2905 AAGCCTGGGA GCCGGCGGGA GGTCTGCCAG GCTGTCCCGT GCCCTGCTCG GTGGCAGTAC AAGCTGCGCG CCTGCAGCGT
TTCGGACCCT CGGCCGCCCT CCAGACGGTC CGACAGGGCA CGGGACGAGC CACCGTCATG TTCGACCGCC GGACGTCGCA
+1 S C G R G V V R R I L Y C A R A H G E D D G E E I L
2985 GAGCTGTGGG AGAGGGGTCG TGCGGAGGAT CCTGTATTGT GCCCGGGCCC ATGGGGAGGA CGATGGTGAG GAGATCCTGT
CTCGACACCC TCTCCCAGC ACGCTCCTA GGACATAACA CGGGCCCGGG TACCCTCCT GCTACCACTC CTCTAGGACA
+1 L D T Q C Q G L P R P E P Q E A C S L E P C P P R W K
3065 TGGACACCCA GTGCCAGGGG CTGCCTCGCC CGGAACCCCA GGAGGCGCTGC AGCCTGGAGC CCTGCCCACC TAGGTGAAAA
ACCTGTGGGT CACGGTCCCC GACGGAGCGG GCCTTGGGGT CCTCCGGAGC TCGGACCTCG GGACGGGTGG ATCCACCTTT
+1 V M S L G P C S A S C G L G T A R R S V A C V Q L D Q
3145 GTCATGTCCC TTGGCCCATG TTCGGCCAGC TGTGGCCTTG GCACTGCTAG ACGCTCGGTG GCCTGTGTGC AGCTCGACCA
CAGTACAGG AACCGGGTAC AAGCCGGTCG ACACCGGAAC CGTGACGATC TCGAGCCAC CGGACACAG TCGAGCTGTT
+1 G Q D V E V D E A A C A A L V R P E A S V P C L I A
3225 AGGCCAGGAC GTGGAGGTGG ACGAGGCGGC CTGTGCGGCG CTGGTGCGGC CCGAGGCCAG TGTCCCTGT CTCATTGCCG
TCCGGTCTG CACCTCCACC TGCTCCGCCG GACACGCCGC GACCACGCCG GGCTCCGGTC ACAGGGGACA GAGTAACGGC
+1 D C T Y R W H V G T W M E C S V S C G D G I Q R R R D
Thrombospondin Submotif
=====
3305 ACTGCACCTA CGCTGGCAT GTTGGCACCT GGATGGAGTG CTCTGTTTCC TGTGGGGATG GCATCCAGCG CCGGCGTGAC
TGACGTGGAT GCGGACCGTA CAACCGTGA CCTACCTCAC GAGACAAAGG ACACCCCTAC CGTAGGTCGC GGCCGCACTG
+1 T C L G P Q A Q A P V P A D F C Q H L P K P V T V R G
Thrombospondin Submotif
=====
3385 ACCTGCCTCG GACCCAGGC CCAGGCGCCT GTGCCAGCTG ATTTCTGCCA GCACTTGCCC AAGCCGGTGA CTGTGCGTGG
TGGACGGAGC CTGGGGTCCG GGTCCGCGGA CACGGTCGAC TAAAGACGGT CGTGAACGGG TTCGGCCACT GACACGCACC
+1 C W A G P C V G Q G T P S L V P H E E A A A P G R T
Thrombospondin Submotif
=====
3465 CTGCTGGGCT GGGCCCTGTG TGGGACAGGG TACGCCCAGC CTGGTGCCCC ACGAAGAAGC CGTGCTCCA GGACGGACCA
GACGACCCGA CCCGGGACAC ACCCTGTCCC ATGCGGGTCG GACCACGGGG TGCTTCTTCG GCGACGAGGT CTGCGCTGGT
+1 T A T P A G A C G R Q H L E P T G T I D M R G P G Q A
3545 CAGCCACCCC TGCTGGTGCC TGTGGCAGGC AGCACCTTGA GCAACAGGA ACCATTGACA TGCAGGGCCC AGGGCAGGCA
GTCGGTGGGG ACGACCACGG ACACCGTCCG TCGTGGAAC TCGTTGTCTT TGGAACCTGT ACGCTCCGGG TCCCGTCCGT
+1 D C A V A I G R P L G E V V T L R V L E S S L N C S A
3625 GACTGTGCAG TGGCCATTGG GCGGCCCTC GGGGAGGTGG TGACCCTCG CGTCCTTGAG AGTTCTCTCA ACTGCAGTGC
CTGACACGTC ACCGGTAACC CGCCGGGGAG CCCCTCCACC ACTGGGAGGC GCAGGAACCTC TCAAGAGAGT TGACGTCACG
+1 G D M L L L W G R L T W R K M C R K L L D M T F S S
3705 GGGGGACATG TTGCTGCTTT GGGGCCGGCT CACCTGGAGG AAGATGTGCA GGAAGCTGTT GGACATGACT TTCAGCTCCA
CCCCCTGTAC AACGACGAAA CCCCGGCCGA GTGGACCTCC TTCTACAGT CTTTCGACAA CTGTACTGA AAGTCGAGGT
+1 K T N T L V V R Q R C G R P G G G V L L R Y G S Q L A
3785 AGACCAACAC GCTGGTGGTG AGGCAGCGCT GCGGGCGGCC AGGAGGTGGG GTGCTGCTGC GGTATGGGAG CCAGCTTGCT
TCTGTTGTG CGACCACCAC TCCGTCGCGA CGCCCGCCG TCCTCCACCC CACGACGAC CCATACCTC GGTGCAACGA

09/836,712
10/9/12

+1 P E T F Y R E C D M Q L F G P W G E I V S P S L S P A
3865 CCTGAAACCT TCTACAGAGA ATGTGACATG CAGCTCTTTG GGCCCTGGGG TGAAATCGTG AGCCCTCGC TGAGTCCAGC
GGACTTTGGA AGATGTCTCT TACACTGTAC GTCGAGAAAC CCGGGACCCC ACTTTAGCAC TCGGGGAGCG ACTCAGGTCC

+1 T S N A G G C R L F I N V A P H A R I A I H A L A T
3945 CACGAGTAAT GCAGGGGGCT GCCGGCTCTT CATTAAATGTG GCTCCGCACG CACGGATTGC CATCCATGCC CTGGCCACCA
GTGCTCATTA CGTCCCCCGA CGGCCGAGAA GTAATTACAC CGAGGCGTGC GTGCCTAACG GTAGGTACGG GACCGGTGGT

+1 N M G A G T E G A N A S Y I L I R D T H S L R T T A F
4025 ACATGGGCGC TGGGACCGAG GGAGCCAATG CCAGCTACAT CTTGATCCGG GACACCCACA GCTTGAGGAC CACAGCGTTC
TGTACCCGCG ACCCTGGCTC CCTCGGTTAC GGTGATGTA GAACTAGGCC CTGTGGGTGT CGAACTCCTG GTGTGCAAG

+1 H G Q Q V L Y W E S E S S Q A E M E F S E G F L K A Q
4105 CATGGGCAGC AGGTGCTCTA CTGGGAGTCA GAGAGCAGCC AGGCTGAGAT GGAGTTCAGC GAGGGCTTCC TGAAGGCTCA
GTACCCGTCG TCCACGAGAT GACCCTCAGT CTCTCGTCGG TCCGACTCTA CCTCAAGTCG CTCCCGAAGG ACTTCCGAGT

+1 A S L R G Q Y W T L Q S W V P E M Q D P Q S W K G K
4185 GGCCAGCCTG CGGGGCCAGT ACTGGACCCT CCAATCATGG GTACCGGAGA TGCAGGACCC TCAGTCCTGG AAGGGAAAGG
CCGGTCGGAC GCCCCGGTCA TGACCTGGGA GGTAGTACC CATGGCCTCT ACGTCCTGGG AGTCAGGACC TTCCTTTCC

+1 E G T
4265 AAGGAACC
TTCCTTGG

003613-044704

Metalloproteinase Domain Alignment of ADAMTS-M v. ADAMTS Family

		Percent Homology	
		Sim	Ident
301	360		
hadAMTS-4 (AB014588)	(202) SPSPRR--	44	32
hadAMTS-5 (AF142099)	(241) QSALSAGGSGPQTWRRRSISRAEQ--	44	28
hadAMTS-1 (AF060152)	(220) QGVGQGTGTSI---	47	23
hadAMTS-8 (AF060153)	(199) ASEPPPLGATS---	46	23
hadAMTS-2 (AJ003125)	(248) ERANSR--R---	49	32
M1-MPD	(1) -----		
Consensus	(301) P R KRFAS R VETLLVAD SMA FHG GLQ YLLTLMSTAA	63	48
361	420		
hadAMTS-4 (AB014588)	(251) KAFKHE--		
hadAMTS-5 (AF142099)	(299) RYKSHR--		
hadAMTS-1 (AF060152)	(274) RYKSHR--		
hadAMTS-8 (AF060153)	(253) RYKSHR--		
hadAMTS-2 (AJ003125)	(300) ELKHE--		
M1-MPD	(39) ELKHE--		
Consensus	(361) RLYKHPSI N I LVVVK VIL D GPEV NAA TLRNFC WQ N P D HPEH		
421	480		
hadAMTS-4 (AB014588)	(310) F PAMIE--		
hadAMTS-5 (AF142099)	(358) F PAMIE--		
hadAMTS-1 (AF060152)	(333) F PAMIE--		
hadAMTS-8 (AF060153)	(312) F PAMIE--		
hadAMTS-2 (AJ003125)	(360) F PAMIE--		
M1-MPD	(98) F PAMIE--		
Consensus	(421) YDTAILFTQQDLG G CDTLGMADVGT CDP RSC VIEDDGLQAFT AHELGHVIG		
481	540		
hadAMTS-4 (AB014588)	(369) IL--		
hadAMTS-5 (AF142099)	(417) IL--		
hadAMTS-1 (AF060152)	(392) IL--		
hadAMTS-8 (AF060153)	(372) IL--		
hadAMTS-2 (AJ003125)	(416) IL--		
M1-MPD	(158) IL--		
Consensus	(481) M HDSPC S SL GP HVMAS D PWSPCS A IT FLD GHG CLLD P		

09/836,712
12 g/12

541
HADAMTS-4 (AB014588) (429) EAP--LHEVTFFG--KDYDADRCQQLFFGPPSRHCP--OLPPPCAAFWGSGHLNCHAMC 600
HADAMTS-5 (AF142099) (476) RKQ--ILCFEEFFG--OTTDATQCNLFTEPEYSVEH--GMDVCAFWGAVVRQOMVE
HADAMTS-1 (AF060152) (451) QNP--IOFFGDFPG--TSYDANRCQFFGEGSKHCP--DAASTCSFWGCTGTSGVIVC
HADAMTS-8 (AF060153) (431) GAA--LPFTGTEGRVALKQLDQCGRQIFGPDFFRCHENTSAQDVCAQLWCH-TDGAEPLE
HADAMTS-2 (AJ003125) (471) FPHDPALE-QFFG--LHMSNNEGRFDEGLSYMMCTAFRTFFPKQWGS-HPDNYPFG
(213) RP-----
MI-MPD
Consensus (541) A LP LPG YDA QC TFGPD HCP D CA LWC G C